Identification and Characterization of Stem Cells in the Posterior Midgut of Adult *Drosophila melanogaster*

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The mammalian gut has long been a model system for the study of stem cell biology. In order to expand our knowledge of gut stem cell biology, we have begun to study the adult midgut of *Drosophila melanogaster*. Remarkably, we have found that the *Drosophila* midgut has stem cells and that they behave strikingly similar to mammalian gut stem cells. The *Drosophila* adult midgut is composed of a simple epithelium surrounded by a layer of muscle. Through pulse-chase labeling experiments, we discovered that the posterior midgut epithelium is completely regenerated in approximately a week. This result argues for the existence of stem cells in the gut that give rise to progeny that replace cells lost through turnover. The epithelium is made up of nests of 2 to 3 diploid cells interspersed among large polyploid cells (enterocytes) and pairs of neuroendocrine cells. In order to identify the location and behavior of stem cells, we made marked clones. Our analysis of clones has revealed a number of salient features about stem cells in the posterior midgut. Stem cells are located within the nests of diploid cells and their nuclei are found closer to the basement membrane than the other diploid cells. As in the mammalian gut, stem cells give rise to both enterocytes and neuroendocrine cells; however, they do so without any transient amplification.

The regulation of gut stems in *Drosophila* shows several interesting differences from that previously shown with *Drosophila* ovarian and testis stem cells. Only a fraction of stem cells are active at any given time, and these active stem cells and their progeny are able to inhibit the activity of neighboring stem cells. Interestingly, we were unable to identify any fixed epithelial cell that might provide a niche for stem cells. This raises the possibility that an acellular niche maintains stems cells in the midgut or alternatively that the cells of the surrounding muscle layer act as a niche for stem cells.

Our works establishes the posterior midgut of *Drosophila melanogaster* as an excellent model system to study gut stem cell biology and is likely to reveal important insights into the behavior of mammalian gut stem cells as well.